

TRANSLATION**PATENT COOPERATION TREATY****PCT****INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N0419SP01W	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2004/013627	International filing date (day/month/year) 17.09.2004	Priority date (day/month/year) 22.09.2003
International Patent Classification (IPC) or national classification and IPC A61K31/606, 47/02, 47/12, 47/20, 47/22,		
Applicant NISSHIN KYORIN PHARMACEUTICAL CO., LTD.		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>2</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report																								
Name and mailing address of the IPEA/JP	Authorized officer																								
Facsimile No.	Telephone No.																								

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-17 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. 5, 9-11 _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* 13 _____ received by this Authority on 10.02.2005
- nos.* 1, 3-4, 10, 12 _____ received by this Authority on 28.10.2005
- ☒ the drawings:
- sheets 1-3 _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☒ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☒ the claims, nos. 2 _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1, 3-13	YES
	Claims		NO
Inventive step (IS)	Claims	5-6, 13	YES
	Claims	1, 3-4, 7-12	NO
Industrial applicability (IA)	Claims	1, 3-13	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
<p>Document 1: Joan Jensen, "Identification of major degradation products of 5-aminosalicylic acid formed in aqueous solutions and in pharmaceuticals", International Journal of Pharmaceutics, 1992, Vol. 88, pages 177 to 187</p> <p>Document 2: JP 10-15032 A (Nisshin Flour Milling Co., Ltd.), 20 January 1998</p> <p>Document 3: US 2442461 A (Walter Karrer), 1 June 1948</p> <p>Document 4: WO 01/85147 A2 (Eli Lilly and Company), 15 November 2001</p> <p>Document 5: JP 8-81360 (Wakamoto Pharmaceutical Co., Ltd.), 26 March 1996</p> <p>Document 6: JP 3-47121 A (Takeda Chemical Industries, Ltd.), 28 February 1991</p> <p>Document 7: Iyaku hin Tenkabutsu Jiten, The Yakuji Nippo Limited, 1st Ed., 1994, pages 59 and 60, 62, 80, 138, 148, 184 and 185, 198 and 199</p> <p>(1) The inventions set forth in claims 1, 3 and 4, and 7 to 12 do not involve an inventive step in the light of documents 1 to 6 cited in the international search report and newly cited document 7.</p>			

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
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Documents 1 and 2 indicate that 5-aminosalicylic acid is discolored by light, oxidation, moisture and steam and the like, and that it is possible to suppress this discoloration by using an absorbent (document 1, summary; document 2, paragraph [0007]).

Meanwhile, as set forth in document 2 (paragraph [0014]), documents 3 to 6 and document 7 (pages 59 and 60, 62, 80, 138, 148, 184 and 185, 198 and 199), thiol compounds, sulfide compounds, fatty carboxylic acid and inorganic salts and the like are commonly used as stabilizing agents in pharmaceutical preparations, and said stabilizing agents are known to have absorbent and antioxidant properties.

It would therefore be easy for a person skilled in the art to conceive of mixing in a stabilizing agent having absorbent activity and antioxidant activity, such as those disclosed in documents 2 to 7, to 5-aminosalicylic acid being easily discolored by light, oxidation, moisture and steam, in order to prevent discoloration.

Moreover, the embodiments set forth in the description of this application merely indicate that specific stabilizing agents such as thiomalic acid and L-cysteine which are known to have antioxidant activity offer a superior discoloration prevention rate for 5-aminosalicylic acid compared to other antioxidants such as sodium bisulfite, sodium pyrosulfite, ascorbic acid and sodium edetate, and it is impossible to confirm that an equivalent effect is offered when using other discoloration preventing agents. In addition, the embodiments indicate that phthalic anhydride, magnesium chloride and the like offer an effect of preventing

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discoloration of 5-aminosalicylic acid, but it is impossible to confirm a superior effect compared to other absorbents, therefore a person skilled in the art would be able to predict said effect in the light of documents 1 to 7.

It would therefore not be particularly difficult for a person skilled in the art to predict the effect of the inventions set forth in claims 1, 3 and 4 and 7 to 12.

(ii) The inventions set forth in claims 5, 6 and 13 are not disclosed in any of the documents cited in the international search report, and are therefore novel and involve an inventive step. In particular, documents 1 to 7, which are acknowledged to be the documents most closely related to prior art, do not indicate that specific stabilizing agents such as thiomalic acid and L-cysteine, which are known to have antioxidant activity, offer a superior discoloration prevention rate for 5-aminosalicylic acid compared to other antioxidants such as sodium bisulfite, sodium pyrosulfite, ascorbic acid and sodium edetate.